

Clinical Experience With Fluether* Anesthesia

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THE ELUCIDATION of the anesthetic properties of Fluothane® by Raventos⁶ in 1956 marked the introduction of one of the most potent and versatile agents into modern anesthesia. There is no doubt that Fluothane® is already firmly established as a major anesthetic as evidenced by the thousands of reported cases in which it was used, and undoubtedly many more thousands unreported. In 1958 Hudon,⁴ reporting on the use of a mixture of Fluothane® and diethyl ether, suggested that the clinical advantages of this mixture included ease of management, less depression of blood pressure and of respiration as compared with pure Fluothane® anesthesia. This mixture of two volumes of Fluothane® and one volume of diethyl ether is described as an azeotrope although it more closely resembles a compound in the liquid state, vaporizes in a fixed ratio identical to that of the liquid residue—that is, two volumes of Fluothane® vapor to one volume of ether vapor. For ease of reference, this mixture is termed “fluether.”

Our use of fluether was undertaken not to assess a substitute or alternative for any existing agent but to evaluate this mixture clinically as an additional anesthetic agent. To assess fluether clinically it must be compared under conditions similar to those in which existing anesthetic agents are used, although purposeful comparison is not the basis of this report. It is the intent of our anesthesia method when using any agent to provide only a light level of anesthesia and to secure muscular relaxation as needed by supplemental use of nonanesthetic relaxant drugs. It is rarely, if ever, our aim to attempt to provide both analgesia and relaxation with one drug or agent. We believe that true anesthesia of sufficient depth to provide profound muscular relaxation will provoke more severe physiological changes of a deleterious nature than will the so-called “light anesthesia” plus relaxants.

Material

Fluether was used in approximately a thousand cases in a period of 14 months: Our clinical experience covers all age groups (the youngest patient,

• Fluether, an azeotropic mixture of two volumes of Fluothane® and one volume of diethyl ether, will provide satisfactory surgical anesthesia in a range of vapor concentration from 0.5 per cent v/v to 4.0 per cent v/v. The agent was used in all age groups and in all patient physical states in approximately a thousand cases.

To date there have appeared no contraindications to the use of fluether anesthesia.

Bradycardia is common during induction but is easily reversible by use of belladonna compounds.

During maintenance of anesthesia, significant muscular relaxation is provided, without evidence of electrocortical depression.

Respiratory depression accompanies a maintenance level of anesthesia.

Recovery after anesthesia with fluether is rapid but tranquil. Considerable analgesia persists during recovery.

36 hours) and all physical states and circumstances of operation, from “healthy, elective” to the “critical, emergency.” With the exception of cardiopulmonary by-pass procedures and obstetrical procedures, surgical operations of all types are included in this report.

Apparatus

In most of the early cases a Fluotec® vaporizer was used to deliver a controlled vapor concentration to a non-return circuit. As experience was gained, other vaporizers and other circuits were employed. At present, fluether is administered in semi-closed, closed, and non-return circuits using a variety of vaporizers, such as the Ohio Vernitrol®, Foregger Copper Kettle®, Ohio Fluothane Vaporizer® and Fluotec®. It should be noted that all these circuits are assemblies of the “out-of-circle” type. Fluether has also been used by catheter insufflation for bronchoscopy and for laryngoscopy.

Using assemblies of the “out-of-circle” type as mentioned above, the expression of per cent fluether vapor as it appears in subsequent paragraphs refers only to the concentrations delivered from the anesthesia machine to the patient breathing circuit. When a closed or semi-closed breathing circuit is employed, this measured vapor concentration will be altered by the admixture of the patient’s exhalations, and the actual inhaled gas will be of unknown vapor concentration.

*An azeotropic mixture of two volumes of Fluothane® and one volume of diethyl ether.

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Induction

The induction is smooth and rapid, both in children and in adults, although in the latter patients a sleep dose of thiobarbiturate is usual. There is noticeable absence of salivation during induction, a circumstance well appreciated in pediatric anesthesia. There is no respiratory rejection of the vapor by the patient and maximum induction concentrations (up to 4 per cent v/v or 5 per cent v/v) can be delivered after a few breaths without irritation or breath holding. Intubation can be performed easily after a fluether induction, pharyngeal and laryngeal reflexes being remarkably quiescent. It is more usual to use succinylcholine to facilitate direct oral intubation in both adults and children, and there seems to be no reason to withhold this drug in any case in which its use might obviate even a remote possibility of injury.

Induction concentrations of 3 per cent volume-for-volume to 4 per cent v/v are delivered from the vaporizer with a half-and-half mixture of oxygen and nitrous oxide at a total diluent flow rate of 4 to 5 liters per minute. This induction concentration of vapor and diluent flow is continued for about ten minutes, provided the blood pressure change is not extreme. As with Fluothane® anesthesia, the calm, quiet induction of fluether may give a false impression of depth of anesthesia and too early stimulation will provoke a very vigorous response. During induction some pulse rate slowing is fairly common; atropine or other belladonna compounds are used early and in sufficient doses to provide a suitable increase in heart rate.

During some phase of the induction, frequently in the early minutes, there will usually be mild to moderate depression of the blood pressure as compared with the pressure before anesthesia. Abrupt and profound hypotension as seen occasionally with Fluothane® induction has not been apparent when using fluether in comparable concentration. The occurrence of moderate depression of blood pressure signals the end of delivery of higher fluether concentrations but does not, per se, indicate anesthesia of sufficient degree to permit surgical stimulation; rather, this agent, as indeed any agent, must be delivered over a variable but sufficient time before adequate anesthesia will result. This blood pressure depression is used only as a guide for the proper setting of the vaporizer control to maintain the desired depth of anesthesia. The limit of the blood pressure depression is planned to be about 30 mm. of mercury below the pre-anesthetic reading in normotensive subjects. If this limit is considered excessive for any patient—as it might be for, say, a patient in shock or one with heart disease or hypertension—or if the limit is grossly exceeded, reduc-

tion in the concentration of fluether vapor delivered will readily reverse the decrease in pressure. The intravenous injection of atropine at this time will also help to elevate the blood pressure. Rarely, have we found vasopressor agents necessary, and use of them is becoming even less frequent as we gain in experience in the use of this anesthetic. After the period of induction at high total gas flows, there is adequate denitrogenization, and reduced total flow for closed circuit technique can be administered if desired.

Maintenance

Maintenance concentration of fluether vapor delivered into circuit will vary from less than 1 per cent v/v to about 3 per cent v/v. The most reliable guide to this concentration is the level and stability of the blood pressure; as previously mentioned, an acceptable vapor concentration usually results in a stable but slightly depressed blood pressure. As in anesthesia using any agent, if maintenance doses of fluether are inadequate, stimulation will result in an elevation of the blood pressure.

When using the Fluotec® vaporizer the total gas flow, whether oxygen alone or a mixture of nitrous oxide and oxygen, is not reduced below one liter per minute, because of variability of the vapor concentrations with this instrument at lower flow rates. With the "Copper Kettle"® and vaporizers of similar type, lower total flow rates are sometimes used, although no persistent attempt is made to provide completely closed-circuit anesthesia in the majority of cases.

Repeated electroencephalographic recordings in cases in which this method of maintenance was used resulted in electrocortical patterns indicative of "light" anesthesia—that is, fast activity (15 to 20 cycles per second) with voltages up to 100 microvolts and only occasional areas of mixed fast and slower patterns. There has been no "burst suppression" attributable to the level of anesthesia. No respiratory stimulation in depth or minute volume has been consistently observed during fluether anesthesia. Light anesthesia with adequate pulmonary ventilation provide optimum conditions in respect to patient physiological response to anesthesia.^{2,3} Fluether anesthesia is accompanied by some respiratory depression and it is our invariable habit to assist or control the ventilation during the course of the anesthesia.

Light anesthesia with fluether will provide appreciable muscular relaxation, usually adequate for major portions of pelvic laparotomy, genito-urinary procedures and other surgical adventures not demanding the cadaveric conditions requested for complicated upper abdominal procedures. If relaxation of a greater degree than that provided by the fluether anesthesia is required or requested, this

additional relaxation is accomplished by the use of succinylcholine, either by intermittent dose method or by continuous drip, depending on the surgical situation. The level of anesthesia is not changed to attempt to provide relaxation in these circumstances; our preference is to maintain a steady state of anesthesia and supplement with succinylcholine as required. The choice of succinylcholine as the relaxant is based on the circumstances involved in its use; namely, requirements for relaxation over and above that which is intrinsic in the anesthesia will be discontinuous as the surgical demands vary, and it seems that a controllable, short-acting agent would most specifically meet the needs of the situation. There has not been any case of "prolonged" apnea with the use of fluether and succinylcholine in this series, even though in some of the cases anesthesia was maintained for 8 or 9 hours.

Termination

When the anesthesia has been of such duration that a stable plasma level of drug can reasonably be assumed (that is, when there is equilibrium with a fixed vapor concentration in inspired air), it is desirable to discontinue the delivery of vapor about thirty minutes before the operation is expected to be finished. This early but calculated cessation of vapor administration will avoid the apparently prolonged periods of recovery that have been reported.¹ Although recovery time is a very difficult parameter to evaluate, and no attempt has been made to measure this factor accurately in this series, certainly in cases where the anesthesia has been brief and the operation uncomplicated the recovery time is as short as could be desired. In cases in which the anesthesia is prolonged or the operation of great magnitude, it has been impossible to correlate recovery time with anesthesia method or agent. The emergence from fluether anesthesia is smooth, quiet, and unattended by the abrupt, excited awakening sometimes seen after Fluothane® anesthesia, especially in children. We believe that this tranquil recovery after fluether is indicative of a significant degree of postoperative analgesia. In a few patients observed in the recovery room the incidence of nausea and vomiting was greater after fluether than after Fluothane®, but no statistical analysis on this point was attempted. The occurrence of nausea and vomiting is the common episode coinciding with first few minutes of waking and is rarely repetitive. Persistent vomiting did not occur in this series.

DISCUSSION

The azeotropic mixture of two volumes of Fluothane® and one volume of diethyl ether has been used satisfactorily for over a year in many varieties of circumstances.

In the decision as to what method and agent to use for anesthesia, certain standards should be observed for patient safety and satisfaction as well as for practical ease of management for the anesthesiologist. Among these standards are:

1. Agents should be applicable for use in a vast majority of cases, not restricted by age or physical condition of patient or type of proposed operation.
2. The same agent should be applicable for both induction and maintenance of anesthesia. This is especially referable to pediatric anesthesia.
3. The anesthetic agent and method should not be objectionable to the patient.
4. The anesthesia should be adequate without sacrifice of acceptable oxygen concentrations.
5. The anesthesia should be satisfactory but not at the expense of secondary physiological derangements.
6. Because of the prevalence of various electrical devices in the operating rooms, the preferred anesthesia should be nonexplosive.

At the present state of experience with fluether anesthesia, it is considered that this agent does, in fact, satisfy these standards for use.

There have been no circumstances so far encountered that prohibit or restrict the use of fluether anesthesia. The induction of anesthesia is smooth, rapid, and pleasant for the patient; emergence is quiet and not so abrupt as to create excitement. Significant analgesia appears to accompany the emergence, lessening the need for sedation in the immediate postoperative period. Maintenance of anesthesia can be provided with fluether vapor concentrations of from less than 1 per cent v/v to 3 per cent v/v and therefore the diluent can contain any portion of oxygen that is desired up to approximately 96 or 98 per cent. Fluether vapor is compatible with all other anesthetic agents in common use today, also with all relaxants although some restrictions pertain to the use of d-tubocurarine because of the additive effects of Fluothane®, ether and the curare.⁷ The vapor is stable in the presence of soda lime. Severe hypotension has not occurred in degree or frequency to compare with similar experience using Fluothane®. Possibly this reflects the stimulating effect of the ether fraction on the autonomic system and partial compensation of the pronounced hypotensive properties of Fluothane®.⁵

In the range of anesthesia concentrations, the vapor is nonexplosive and therefore there is no restriction on the use of any electrical devices.

The concomitant use of fluether anesthesia and local infiltration with solutions containing epinephrine is discouraged, although this has occurred inadvertently on several occasions without ill effect.

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REFERENCES

1. Adams, A. K., Lambrechts, W., and Parkhouse, J.: Clinical trial of an azeotropic mixture, *Acta Anaesth. Scandinav.*, 3:189, 1959.
2. Dobkin, A. B., Drummond, K., and Purkin, N.: Anesthesia with the azeotropic mixture of halothane and diethyl ether, *Brit. J. Anaesth.*, 31:53, 1959.
3. Dobkin, A. B.: Circulatory dynamics during light halothane anesthesia, *Brit. J. Anaesth.*, 30:568, 1958.
4. Hudon, F., Jacques, A., and Boivin, P. A.: Fluothane-ether: An azeotropic mixture, *Canad. Anaes. Soc. J.*, 5:403, 1958.
5. Price, H. L., Linde, H. W., Jones, R. E., Black, G. W., and Price, M. L.: Sympatho-adrenal responses to general anesthesia in man and their relation to hemodynamics, *Anaesthesiology*, 20:563, 1959.
6. Raventos, J.: The action of fluothane—a new volatile anaesthetic, *Brit. J. Pharmacol.*, 11:394, 1956.
7. Sabawala, P. B., and Dillon, J. B.: Action of volatile anaesthetics on human muscle preparations, *Anaesthesiology* 19:587, 1958.

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